REMARKS

Claims 1-7 and 9-17 are pending in the instant application. A complete Listing of Claims with appropriate status identifier begins on page 17 of this communication.

By the present amendment, Claims 1, 6, 7, 10-14, and 16 have been amended. Unless indicated otherwise, all references herein to the specification refer to the substitute specification submitted September 29, 2005. Support for the amendments can be found, inter alia, throughout the specification and the claims as originally filed. For example, support for the amendment to Claims 1, 7, 14 and 16 can be found in the specification at e.g., page 9, lines 9-11 and 15-16, and page 22, lines 27-28. Support for the amendment to Claims 6 and 11-13 can be found in the specification at e.g., page 21, lines 10-11, and page 22, lines 24-25. Claim 10 has been amended for grammatical considerations only. No new matter is introduced by the amendments provided herewith.

The amendments provided herewith are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and canceled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover, have not acquiesced to any rejections or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Objections to the Specification

Office Action Item 6a)

Applicants respectfully disagree with the Examiner's objection to the specification (Office Action mailed 4/23/2007, page 2, item 6a) as allegedly being unclear with respect to delimiters surrounding the term "SEQ ID NO:." However, in an effort to expedite prosecution, by the present communication the specification has been amended to incorporate parentheses

surrounding sequence identifiers. Accordingly, Applicants respectfully request withdrawal of the present objection.

Office Action Item 6b)

Applicants thank the Examiner for noting (Office Action, item 6b) the typographical error in the date of publication of Arnelo et al, Scan. J. Gastoenterol. 31:83-90 (1996). By the present communication, the specification has been amended to correct the date of publication thereof. Applicants respectfully submit that the typographical error and the correction thereof would be immediately obvious to one of ordinary skill in the art. Accordingly, Applicants respectfully request withdrawal of the present objection.

Office Action Item 8)

The specification was objected to (Office Action, item 8) as allegedly including new matter in the amendment filed December 2, 2002, regarding incorporation by reference to International Application, WPI Acc. No. 93-182488/22. See also Office Action mailed June 1, 2006, item 10(a). Applicants respectfully disagree with this objection.

The CCPA has ruled that in cases of incorporation by reference of essential material, "the applicant will be required to amend the disclosure to include the material incorporated by reference." Application of Hawkins, 486 F.2d 569. Indeed, the specification (page 10, lines 2-3) expressly refers to "[u]seful amylin agonist analogues" found in WPI Acc. No. 93-182488/22. Thus, Applicants respectfully submit that incorporation of the relevant passages of WPI Acc. No. 93-182488/22 is proper.

However, in an effort to reduce the issues and expedite prosecution, by the amendment provided herewith Applicants delete Examples 21-22 of the Substitute Specification filed September 29, 2005, which examples contemplate SEQ ID NO:25 and SEQ ID NO:24, respectively. Applicants note that Table II contemplates peptides having SEQ ID NO:1-15, rather than merely SEQ ID NO:4-15 as asserted by the Examiner (Office Action, item 8, line 13). Accordingly, Applicants respectfully submit that incorporation by reference of Examples 9-20 by the amendment filed December 2, 2002, is proper under Application of Hawkins (id.). Accordingly, Applicants respectfully request reconsideration and withdrawal of the objection.

Provisional rejections under judicially created doctrine of double patenting

Claims 1-6 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting (Office Action, page 4, item 16) as allegedly being unpatentable over the claims of co-pending U.S. Pat. Application No. 09/445,517 (hereinafter "the '517 application"). Claims 7, 13, 14 and 16 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting (Office Action, page 5, item 17) as allegedly being unpatentable over claim 33 of the '517 application. Claims 7, 14 and 16 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting (Office Action, page 5, item 18) as allegedly being unpatentable over claim 6 of co-pending U.S. Pat. Application No. 10/851,574 (hereinafter "the '574 application").

With regard to the provisional rejections, Applicants are willing to consider submitting a terminal disclaimer in the present application with regard to the '517 application and the '574 application should these applications issue as a patent prior to the present application. Accordingly, Applicants respectfully request that the current provisional rejections be deferred pending resolution in the '517 and '574 patent applications.

Rejections under judicially created doctrine of obviousness-type double patenting

Claims 7, 14, 16 and 17

The rejection of Claims 7, 14, 16 and 17 (Office Action, item 38) under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 34 and 35 of U.S. Pat. No. 5,686,411 ("'411 patent") as evidenced by Tsanev (Vutr. Boles 23:12-17, 1984, abstract), is respectfully traversed.

As acknowledged by the Examiner (Office Action, item 38), Claims 34 and 35 of the '411 patent are directed to methods for the treatment of diabetes mellitus in a mammal comprising the administration to said mammal of a therapeutically effective amount of a particular amylin agonist analogue.

In contrast, Claims 7, 14, 16 and 17 of the instant application as currently amended are directed to methods for treating obesity in a human subject in need of such treatment, which methods require administration of a composition or compound containing an amylin or an amylin agonist, wherein the amount of the composition or compound administered is effective to treat

obesity by inhibiting weight gain or inducing weight loss, and wherein the subject is in need of treatment for obesity. Specifically, Claim 7 is directed to a method for treating obesity by administering a composition comprising an obesity relief agent consisting of an amylin or an amylin agonist and a pharmaceutically acceptable carrier. Claim 14 is directed to a method of treating obesity through administering a compound selected from the group consisting of an amylin, an amylin agonist, and salts thereof, wherein the compound is not administered in conjunction with another obesity relief agent. Claim 16 is directed to a method for treating obesity by administering a composition consisting essentially of an amylin or an amylin agonist. Claim 17, dependent on any of Claims 7, 14 or 16, requires a particular amylin agonist.

Regarding the claimed invention, the cited claims of the '411 patent are silent with regard to treating obesity. Indeed, even if obesity is common among those with diabetes, a claim to treating diabetes mellitus with an amylin agonist analogue does not necessarily teach or suggest treating patients with obesity as claimed. Further, nothing in the cited claims teaches or suggests the use of an amylin or an amylin agonist in an amount effective to treat obesity. Yet further, nothing in the cited claims teaches or suggests the identification of a subject in need of treatment for obesity. Specifically, the courts have held that the phrase "in need thereof" (e.g., as recited in independent Claims 1, 7, 14 and 16) is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." Jansen v. Rexall Sundown, Inc. 342 F.3d 1329, 1333 (Fed. Cir. 2003). Thus, since the cited claims do not teach or suggest treating obesity, the population in need of treatment for obesity, or the use of an amount effective to treat obesity, a skilled artisan would have no expectation of success for the claimed invention in view of the cited claims.

In an attempt to cure the deficiency in Claims 34 and 35 of the '411 patent, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. The Examiner further asserts (Office action, page 9, lines 21-23) that "the method of the '411 patent comprising the administration of 0.1 to 5 mg, 0.5 to 1.0 mg or the amylin agonist 25,28,29Pro-human amylin to a diabetic patient anticipates the instant claims (emphasis added)."

Applicants disagree with the Examiner's assertion of inherent anticipation. Anticipation based on inherency is appropriate only when the prior art relied upon necessarily includes all of

the elements of the claims in question, Atofina v. Great Lakes Chemical Corp., 441 F.3d 991, 78 USPQ2d 1417, 1424 (Fed. Cir. 2006), and is the natural result of following the instructions or examples of the prior art. SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1334, 74 USPQ2d 1398, 1407 (Fed. Cir. 2005) (citing Schering Corp. v. Geneva Pharms., Inc., 339 F. 3d 1373, 1377, 67 USPQ2d 1664, 1667 (Fed. Cir. 2003)). The Court in Schering relied in part on the decision In re Cruciferous Sprouts Litigation, 301 F.3d 1343, 1351, 64 USPQ2d 1202, 1206 (Fed. Cir. 2002) wherein it was noted that to demonstrate inherency, it was necessary to show that the prior art necessarily, always functions in accordance with the claims addressed. The requirement that the teaching of a reference always, under any circumstances, necessarily satisfies the recitation of the claims to make out a case of inherent anticipation was reaffirmed by the Federal Circuit in Abbott Laboratories v. Baxter Pharmaceutical Products, Inc., 471 F.3d 1363, 1368 (Fed. Cir. 2006). It is well settled that a determination of inherency cannot be established by probabilities or possibilities, but that it is incumbent upon the Examiner to establish the inevitability of the inherency which is propounded. In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981); In re Wilding, 535 F.2d 631, 635-36, 190 USPQ 59, 63-64 (CCPA 1976).

As acknowledged by the Examiner (Office Action, item 38), Tsanev discloses that 80-90% of diabetic patients are obese. Accordingly, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the present claims and required by the law. Accordingly, Claims 34 and 35 of the '411 patent do not support prima facie obviousness with regard to the claimed invention, and Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 7, 14 and 16

The rejection of Claims 7, 14 and 16 (Office Action, page 9, item 39) under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 11 and 13 of U.S. Pat. No. 5,321,008 ("the '008 patent") as evidenced by Tsanev (Id.) and by U.S. Pat. No. 5,739,106 ("the '106 patent"), is respectfully traversed.

As noted above, Claims 7, 14, and 16 as currently amended are directed to methods for treating obesity in a human subject in need of such treatment through administration of a

composition or compound containing an amylin or an amylin agonist. Furthermore, the courts have held that the phrase "in need thereof" (e.g., as recited in independent Claims 1, 7, 14 and 16) is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." Jansen v. Rexall Sundown, Inc. 342 F.3d 1329, 1333 (Fed. Cir. 2003). In contrast, Claim 11 of the '008 patent is directed to a method for the treatment of diabetes mellitus in an insulin-requiring mammal comprising administering to the mammal a therapeutically effective amount of a calcitonin, where the mammal is a human. Further, Claim 13 of the '008 patent is directed to the method of treatment of type II diabetes mellitus comprising the step of administering a therapeutically effective amount of an insulin and a calcitonin where the ratio of insulin to calcitonin from about 100:1 to about 1:2 and is effective to achieve improved glycemic control over insulin therapy alone.

Furthermore, the cited claims of the '008 patent are silent with regard to treating obesity. Even if obesity is common among those with diabetes, a claim to treating diabetes mellitus does not necessarily teach or suggest treating patients with obesity as claimed. Similar to the rejection based on the '411 patent above, the Examiner's attempts to cure the deficiencies of the '008 patent by citing the alleged prevalence of intrinic obesity (80-90% according to Tsanev), which assertion falls short of the 100% required by the claims and required by the law. Furthermore, since the cited claims do not teach or suggest treating obesity or the use of an amount effective to treat obesity, a skilled artisan would have no expectation of success for the claimed invention in view of the cited claims. Thus, claims 11 and 13 of the '008 patent do not support prima facie obviousness with regard to the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Rejection under 35 U.S.C. §112, first paragraph (New Matter)

Claim 14

The rejection of Claim 14 (Office Action, items 19 and 40) under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter (new matter rejection) which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is respectfully traversed..

Although Applicants disagree with these new matter rejections, Claim 14 has herein been amended in order to facilitate disposition of the present case. As amended, Claim 14 requires a method of treating obesity in a human subject comprising administering to the subject a compound selected from the group consisting of an amylin, an amylin agonist, and salts thereof, wherein the compound is administered in an amount effective to inhibit weight gain or induce weight loss, wherein the subject is in need of treatment for obesity, and wherein the compound is not administered in conjunction with another obesity relief agent. Support for the term "salts" is found throughout the specification at, e.g., page 12, line 25. Accordingly, Applicants request reconsideration and withdrawal of the present rejection.

Claims 9 and 10

The rejection of Claims 9 and 10 (Office Action, page, 11, item 41) under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter (new matter rejection) which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is respectfully traversed. Specifically, Applicants respectfully disagree with the Examiner's assertion (Office Action, page 12 [NB: page 19 in download of Office Action dated April 23, 2007, from PAIR], lines 5-8) that "the specification as originally filed does not provide descriptive support for a composition comprising a pharmaceutically acceptable carrier and an amylin or an amylin agonist as recited being administered QID or TID."

The current rejection appears related to the term "composition" introduced into then-new Claims 9 and 10 in the response dated December 2, 2002. As well understood by one of ordinary skill in the art, compositions useful in the invention necessarily contain the amylin or amylin agonist contemplated in Claims 9 and 10. Indeed, parenteral administration requires formulation into a composition. Furthermore, express support for the term "composition" contemplated for use in the methods of the invention is found in the specification, at e.g., page 21, lines 3-5: "Compositions useful in the invention may conveniently be provided in the form of formulations suitable for parenteral (including intravenous, intramuscular and subcutaneous) or nasal or oral administration." Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 1, 7 and 16

The rejection of Claims 1, 7 and 16 (Office Action, item 42) under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter (new matter rejection) which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is respectfully traversed.

As discussed above relating to the rejection of Claims 9 and 10 (Office Action, page 11, item 41), the specification and claims as originally filed contemplate compositions in Claims 1, 7 and 16 which contain an amylin or amylin agonist of the invention. Furthermore, express support for the term "composition" contemplated for use in the methods of the invention is found in the specification, at e.g., page 21, lines 3-5 (supra). Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection(s) under 35 U.S.C. §112, first paragraph (Scope of Enablement)

The rejection of Claims 1-7 and 9-17 under 35 U.S.C. § 112, first paragraph (Office Action, page 14, item 43), for alleged lack of enablement is respectfully traversed.

The proper standard for determining compliance with the enablement requirement is whether the specification provides sufficient information to permit one skilled in the art to make and use the claimed invention. *United States v. Telectronics, Inc*., 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). The test of enablement is not whether experimentation is necessary, but rather whether any experimentation that is necessary is undue. A considerable amount of experimentation is permitted, provided that it is merely routine, or provided that the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

It is submitted that the Examiner has not met the evidentiary burden to impose an enablement rejection for failure to enable one of skill to use the invention. A specification that discloses how to make and use a claimed invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566,

34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995) (*quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original)).

It is well established that enablement does not require the inventor to submit an exact blueprint or recipe to practice the invention; thus, experimentation is allowed. *In re Angstadt*, 190 USPQ 214 (CCPA 1976). Rather, the determination of what constitutes undue experimentation relies on the Wands factors: (1) the quantity of experimentation necessary (time and expense); (2) the amount of direction or guidance presented; (3) presence of absence of a working example; (4) nature of the invention; (5) the state of the prior art; (6) the relative skills of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *In re Wands*, *Id*.

In rejecting the claims, the Examiner impermissibly attempts to limit the invention to the scope of the examples. Applicants respectfully submit that such a standard is legally incorrect. As set forth in MPEP § 2164.02, "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation." This is exactly what Applicants have provided. For example, Tables I - II and Examples 1-8 disclose data relating to the claimed methods and exemplary amylin compounds. Alone, this disclosure is sufficient such that one of ordinary skill in the art at the time the invention was made would have the ability to practice the invention commensurate in scope with the claims.

Nonetheless, in one aspect, the Examiner has alleged that the specification does not enable treating obesity in *any* human subject, including a non-diabetic or non-type 2 diabetic human subject in need thereof, or a type 2 diabetic human subject in need thereof who is not on insulin therapy. Applicants respectfully traverse. M.P.E.P. § 2164.01(a) states that it is improper to conclude that a disclosure is not enabling based on an analysis of only one of the *Wands* factors while ignoring one or more of the others. "The Examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole." M.P.E.P. § 2164.01(a); *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988). Again, the Examiner appears to have focused his attention almost exclusively on the

working examples, and not on other applicable evidence of enablement. For example, the Examiner has not addressed, among other items, the nature of the invention, the state of the prior art, the level of one of ordinary skill, and the amount of direction provided by the Applicant.

More specifically, the specification broadly teachings that the claimed amylin compounds are useful in the treatment of obesity in a subject in need thereof. There is express guidance as to modes of administration, therapeutic dosages, mechanisms for assessing therapeutic efficacy, as well as a working example to demonstrate the statistically significant ability of an exemplary amylin compound to treat obesity in a human subject in need thereof. In the working example, the human subjects were type-2 diabetics. That the working example illustrated type-2 diabetic subjects taking insulin does not render the scope of enablement limited to this subject population. Rather, it demonstrates that in a particularly difficult to treat, obese subject population (type-2 diabetic subjects taking insulin), an exemplary amylin compound is therapeutically effective in the treatment of obesity - independent of life-style changes and insulin dependence.

Moreover, taken together with the teachings of the specification (e.g., Para. [0095]-[0109]), the working example provides a base-line approach for establishing therapeutic efficacy of exemplary amylin compounds within the context of the presently claimed methods. Utilizing similar study structures, Applicants have in fact established that exemplary amylin compounds are effective in the treatment of obesity in non-diabetic subjects as well (see, *e.g.*, Chapmen, *et al*; Aronne, *et al.*; Smith, *et al.*; *etc.* included in the IDS filed herewith). This evidence confirms the teachings of Applicants specification, and demonstrates that Applicants working example in fact provides enablement of the efficacy of a particularly difficult to treat, chronically obese subject population.

The Examiner also comments on the scope of the claimed amylin compounds, and notes that the "only amylin agonist analogues that was administered in the instant invention" was pramlintide. Applicants respectfully traverse. Again, the Examiner appears to be focusing on working example 1 rather than the teachings of the specification as a whole and the level of ordinary skill in the art. In this regard, it is noted that amylin compounds recited in the claims are generally recognized as a defined class of compounds, and the specification provides ample

direction and guidance to those skilled in the art with regard to the identification of such amylin compounds useful in the context of the claimed methods.

The specification is replete with examples of amylin agonists, including functional variants, fragments, and derivatives of amylin and amylin agonists. See, *e.g.*, *Specification*, Background and Para. [0033]-[0090]. For example, given at least the discussion in the background concerning amylin agonists, as well as the description of SEQ ID NO: 12-17, one of ordinary skill in the art having read the specification would have the ability to select known amylin agonists without undue experimentation. *Id.* Moreover, to the extent that any additional experimentation may be required, Applicant notes that the performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

For instance, given the knowledge in the art, and based on the guidance provided in the specification regarding the extensive exemplary embodiments of amylin compounds, receptor binding assays and other assays for determining amylin activity, including the soleus muscle assay, and exemplary clinical study designs, additional therapeutically active amylin agonists can be identified within the context of the present claims without the need for undue experimentation. The Examiner's attention is respectfully drawn to the lengthy description that provides numerous examples of compounds within the scope of the recited genus, and guidance with regard to assays and clinical studies in the examples useful to evaluate the efficacy of the compounds in the methods of the present invention. Based on such guidance, one of skill in the art would be able to practice the claimed invention with only routine experimentation.

Further, certain of the dependent claims recite specific types of amylin compounds (e.g., amylin agonist analogues including the amylin agonist analogue of SEQ ID NO: 1). As generally understood by those of skill in the art, amylin analogues are compounds that are structurally related to the reference compound, i.e., amylin. As explained in the specification and understood by those skilled in the art, an amylin analogue can have one or more amino acid substitutions, deletions, inversions, or additions compared to a native or naturally occurring amylin. Further, the claims clarify that the amylin analogue is an amylin agonist analogue. Thus, in accordance

with the claims and the knowledge of those of ordinary skill in the art, the recited amylin agonist analogues are both structurally and functionally defined.

In a related comment, the Examiner alleges that the state of art with regard to the use of amylin is unpredictable. In this regard, the Examiner asserts that both Baron *et al.* and Ratner *et al.* indicate the impracticability of using amylin as a therapeutic agent. *Id.* Applicants respectfully disagree. Whether native human amylin is suitable for use as a commercial drug product is not a proper standard for judging the enablement of the present claims.

Moreover, contrary to the Examiner's characterization of the cited references, it is submitted that both Baron *et al*. and Ratner *et al*. actually support enablement of the claimed invention. That is, given the teachings of the instant specification coupled with the teachings of the prior art, one of ordinary in the art would have the ability to select amylin and amylin agonist peptides for use in the claimed methods without undue experimentation. This further confirms that both amylin and amylin agonists are well known compounds that have been widely characterized. Given this, one of ordinary skill in the art would have the requisite skill to practice the invention commensurate in scope with the claims without undue experimentation.

In yet another aspect, the Examiner has also asserted that the specification does not enable administration by *any* route, or administration of "an amount effective to treat obesity" commensurate in scope with the claims. Applicants respectfully traverse. Again, the Examiner is attempting to limit the scope of enablement to the scope of the Applicants' working examples. Based on the extensive guidance provided in the specification, including the human clinical study results, as well as the high level of skill in the art, the skilled artisan would be able to evaluate efficacy of amylin compounds in accordance with the methods of the inventions to ascertain therapeutically effective amounts of the recited amylin compounds. In fact, the Examiner's characterization of working Example I only serves to underscore the enablement of the claims in this regard. For instance, working Example I describes a clinical study wherein routine dosages were evaluated in human clinical subjects to ascertain a therapeutically effective dose as well as effective administration regimens. Further, the standard of enablement is not commensurate with an evaluation of safety and efficacy. Such a task is left to the extensive procedures and oversight of the Food and Drug Administration.

It should be noted that the use of the term "effective amount" coupled with the result to be achieved has been approved by the courts and the Board for over 40 years. *See*, e.g., *In re Caldwell,* 319 F.2d 254 (C.C.P.A. 1963); *In re Halleck,* 422 F.2d 911 (C.C.P.A. 1970); *In re Watson,* 517 F.2d 465 (C.C.P.A. 1975); *In re Skuballa*, 12 U.S.P.Q. 2d 1570 (B.P.A.I 1989). In addition to working Example 1, the specification provides guidance directly on the matter of the determination of appropriate "effective amounts," and discusses suggested useful doses and routes for administration in humans, *e.g.*, at Paras. [0107]-[0108]. Based on such guidance, one of skill in the art would be able to practice the claimed invention with only routine experimentation.

The Examiner also makes numerous comments with regard to the scope of various claim terms and transitional phrases. For instance, various claim terms such as obesity and administering are discussed in a broad context. While applicants do not necessary agree with the exact definition provided by the Examiner, Applicants do acknowledge the broad scope of such terms commensurate with the present specification. Further, the Examiner comments on the claims use of traditional transitional phrases such as "comprising," "consisting of," and consisting essentially of". In this regard, Applicants note that such language have been used in their traditional context. Thus, within the context of the claimed methods for treating obesity, would have their traditional meanings and limitations with regard to claim elements relevant to the treatment of obesity. However, such tradition claim terms would have no bearing on components, steps, or elements outside of the claimed scope of the treatment of obesity.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. § 102:

Anticipation under 35 U.S.C. § 102 can only be found if a reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 780 (Fed. Cir. 1985). Furthermore, anticipation requires that every limitation of the claims be found, either expressly or inherently, in a single prior art reference, device, or practice.

Claims 1, 5, and 7 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Miltz (U.S. Pat. No. 5,220,113).

The Examiner states that, "Miltz discloses an iceberg lettuce cultivar, namely 'BUD 71-3', having a length to width ratio between about 1.2 to about 2.7, namely 1.5, and a color rage from about RHS 146A to about RHS 146B, namely RHS 146B …". The Examiner cites to column 4, line 52, to column 5, line 4, and column 1, line 53, of Miltz for support.

Applicant disagrees.

Applicant respectfully submits that neither column 4, line 52 to column 5, line 4 nor column 1, line 53 of Miltz provides support for the Examiner's contentions. Whatever else Miltz teaches, it does not teach an iceberg lettuce cultivar, or a part thereof, wherein said iceberg lettuce cultivar comprises a first outer leaf having a length to width ratio between about 1.2 to about 2.7 and a color which ranges from about RHS 146A to about RHS 146B. Column 4, lines 61 to 63, at most states that the length/width index of the fourth leaf is 1.5. The Examiner has therefore failed to demonstrate that each and every limitation of the claims is found in Miltz. Therefore, Miltz cannot anticipate claims 1, 5, and 7.

In addition to the arguments set forth above, the Examiner is also mistaken in asserting that claim 5 is within the scope of the Miltz patent. Whatever else Miltz teaches, it does not teach the varieties described therein, and specifically BUD 71-3, have inner leaves meeting the specified color range. The passage relied by the Examiner at most states one common morphological characteristic of Vanguard-type lettuce cultivars is "[h]eads with creamy colored interiors." The Examiner has not, however, established that that description corresponds to a color ranging from about RHS 145C to about RHS 145D. Moreover the Examiner has not even established that BUD 71-3 is a member of the Vanguard-type of cultivar, let alone that it has the specific characteristic mentioned. Thus, to meet the limitations of claim 5, the Examiner is creating a hypothetical cultivar from passages the background of the patent and other passages in the detailed description.

Applicants note the Examiner rejects claims 1, 5, and 7 relying on *In re Thorpe* for the proposition that a product-by-process claim may be properly rejectable over prior art teaching the same product produced by a different process. Office Action of May 3 at page 7. Applicants

respectfully draw the Examiner's attention to the fact that none of claims 1, 5, or 7 is a product-by-process claim.

In an attempt to place the burden of demonstrating novelty and non-obviousness upon Applicants, the Examiner relies upon *In re Best*. Office Action of May 3 at page 7. That reliance is misplaced. The *Best* court stated "[w]here… the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product." *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977). As the Miltz product relied upon by the Examiner, *i.e.*, BUD 71-3, does not even seem to be substantially identical to the claimed product, *In re Best* offers the Examiner no basis upon which to switch the burden to Applicants. Applicants respectfully maintain that they are under no obligation to submit evidence of novelty or non-obviousness under *In re Best* unless and until the Examiner establishes that the claimed invention is at least substantially identical to the product relied upon in Miltz.

Further to the foregoing, Applicants have amended independent claim 1 to recite that the plants have an elliptical stature. The BUD 71-3 variety cited against Applicants' claims is described by Miltz as being spherical at column 5, lines 10-15, and the Examiner admits Miltz does not teach Elliptical shaped heads. Office Action of May 3, 2007, at page 9.

In conclusion, Applicant respectfully submits that claims 1, 5, and 7 are not anticipated by Miltz and respectfully requests withdrawal of this rejection.

Claim 1 was rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Waycott et al. (U.S. Pat. No. 5,973,232).

Applicant respectfully traverses. According to the Examiner, "Waycott *et al*. disclose an iceberg lettuce cultivar, namely 'Sharp Shooter', comprising a length to width ratio between about 1.2 to about 2.7, namely 1.7 …". Office Action at page 8. The Examiner cites to column 2, lines 27-28 and column 5, line 41 of Waycott *et al.* for support. Unfortunately, the teachings at column 2, lines 27-28 and column 5, line 41 either alone or in combination fail to provide support for the Examiner's contentions. The teachings fail as column 5, line 41, states that the length/width index of the fourth leaf is 1.7.

It is axiomatic that in order for a prior art reference to anticipate a claim, the reference must teach every element of the claim. *See*, M.P.E.P. § 2131. Whatever else Waycott *et al.* teach about the shape of the 4th leaf, the do not teach or fairly suggest "[a]n iceberg lettuce cultivar, or a part thereof, wherein said iceberg lettuce cultivar has an elliptical stature and comprises a first outer leaf having a length to width ratio between about 1.2 to about 2.7 and a color which ranges from about RHS 146A to about RHS 146B. Moreover, as noted above, Applicants have amended claim 1 to recite that the plants have an elliptical stature. The stature of the lettuce described by the '113 patent is recited as being spherical at column 6, line 24.

In view of the foregoing, Waycott *et al.* cannot anticipate claim 1.

As in the rejection over, the Miltz reference the Examiner relies on *In re Thorpe* for the proposition that a product-by-process claim may be properly rejectable over prior art teaching the same product produced by a different process. Office Action of May 3 at page 8. Applicants again respectfully draw the Examiner's attention to the fact that claim 1 is not a product-by-process claim.

Moreover, as with the rejection over the Miltz citation, the Examiner's again relies upon *In re Best* in an attempt to place the burden of demonstrating novelty and non-obviousness upon Applicants. Office Action of May 3 at page 8. That reliance misplaced for the same reasons it was misplaced in the Examiner's formulation of the Miltz rejection under section 102(b). As the product relied upon by the Examiner does not even seem to be substantially identical to the claimed invention, *In re Best* offers the Examiner no basis upon which to switch the burden to Applicants. Applicants respectfully submit they are under no obligation to submit evidence of novelty or non-obviousness under *In re Best* unless and until the Examiner establishes that the claimed invention is at least substantially identical to the product relied upon in Waycott.

In conclusion, Applicant respectfully submits that claim 1 is not anticipated by Waycott *et al.* and respectfully requests withdrawal of this rejection.

Rejection(s) under 35 U.S.C. §112, second paragraph

The rejection of Claims 1-7 and 9-17 under 35 U.S.C. §112, second paragraph (Office Action, page 20, item 44), for alleged indefiniteness are respectfully traversed. Responses to specific rejection points follow:

(a) Claim 6 as amended requires a specified amount of an amylin or amylin agonist contemplated therein to be contained in the composition, thereby obviating any alleged vagueness, indefiniteness and confusion asserted in the rejection.

(b) Similar to the argument for Claim 6, Claims 11-13 as amended require specified amount of the amylin or amylin agonist contemplated therein to be contained in the composition.

(c) Applicants thank the Examiner for the grammatical suggestion relating to Claim 10 and have amended Claim 10 accordingly by incorporation of the word "and" as indicated in the amendment.

(d) Claims 1, 7, 14 and 16 as amended require that compounds administered according to the methods of the invention be effective to treat obesity in the human subject, thereby obviating any alleged vagueness or indefiniteness relating to in whom the recited amount is effective to treat obesity.

(e) Applicants submit that Claims 2-6, 9-13, 15 and 17 depend from base claims (i.e., 1, 7, 14 or 16) which are not indefinite in view of the amendments provided herein.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Rejection(s) under 35 U.S.C. §102

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). See also, MPEP §2131. The identical invention must be shown in complete detail as it is contained in the claim. Richardson v. Suzuki Motor Co., 9 USPQ2d 1913 (Fed. Cir. 1989).

Claims 1-7, 9-14, 16 and 17

The rejection of Claims 1-7, 9-14, 16 and 17 under 35 U.S.C. § 102(a) (Office Action, page 20, item 45) for alleged anticipation over Kolterman et al. (WO 96/40220) ("Kolterman '220") as evidenced by Tsanev (Id.) is respectfully traversed.

As noted above, the claimed invention is directed to methods of treating obesity in a human subject in need of such treatment through administration of an amylin or an amylin agonist. In contrast, as acknowleged by the Examiner (Office Action, page 21, lines 14-18), Kolterman ‘220 describes the use of an amylin agonist (i.e., pramlintide) for treating type II

diabetes mellitus. Indeed, Kolterman '220 demonstrates that administration of an amylin agonist significantly reduces postprandial plasma glucose concentrations in patients with type II diabetes mellitus. However, Kolterman '220 does not teach the use of an amylin or an amylin agonist for treating obesity or demonstrate a reduction in body weight in those patients administered an amylin or an amylin agonist. Furthermore, Kolterman '220 is silent with regard to the effect of an amylin or an amylin agonist on body weight. Indeed, the Examiner acknowledges (Office Action, page 23, lines 16-18) that Kolterman '220 is missing descriptive matter relating to obesity in diabetic subjects. In an attempt to cure the deficiency in Kolterman '220, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. However, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the claims and required by the law as discussed in the respone to Office Action item 38 above. See e.g., Schering Corp. v. Geneva Pharms., Inc., Id.; Abbott Laboratories v. Baxter Pharmaceutical Products, Inc., Id.) Thus, Kolterman '220 does not provide each and every element of the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 7, 14, 16 and 17

The rejection of Claims 7, 14, 16 and 17 under 35 U.S.C. § 102(e)(2) (Office Action, page 23, item 46) for alleged anticipation over the '411 patent as evidenced by Tsanev (Id.) is respectfully traversed.

As discussed above in the response to the rejection of Office Action, item 38, the '411 patent is silent with respect to treating obesity, nothing in the '411 patent teaches or suggests the use of an amylin or an amylin agonist in an amount effective to treat obesity, and nothing in the '411 patent teaches or suggests the identification of a subject in need of treatment for obesity. In an attempt to cure the deficiency of the '411 patent, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. Indeed, the Examiner acknowledges a deficiency in the '411 patent relating to missing descriptive material and asserts (Office Action, page 25, lines 2-4) that "the missing descriptive material, i.e., prevalence of 80-90% ob obesity in the diabetic subject, is necessarily present in the thing described by Gaeta et al. ('411)."

However, the law is clear that anticipation based on inherency is appropriate only when the prior art relied upon necessarily includes all of the elements of the claims in question, Atofina v. Great Lakes Chemical Corp. (Id.), and is the natural result of following the instructions or examples of the prior art. See SmithKline Beecham Corp. v. Apotex Corp., (Id.) In the present case, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the claims and required by the law. Accordingly, the '411 patent does not anticipate the claimed invention, and Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 1-7, 9, 11-14, 16 and 17

The rejection of Claims 1-7, 9, 11-14, 16 and 17 under 35 U.S.C. § 102(b) (Office Action, page 25, item 47) for alleged anticipation over Kolterman et al. (Diabetologia, 39:492-499, April 1996; hereinafter "Kolterman 1996") as evidenced by Itasaka et al. (Psychiatr. Clin. Neurosci. 54:340-341) is respectfully traversed.

Kolterman 1996 describes the use of an amylin agonist, pramlintide, for treating patients with insulin-dependent diabetes mellitus and demonstrates that administration of the amylin agonist significantly reduces postprandial plasma glucose concentrations. Kolterman 1996 does not teach the use of the amylin agonist for treating obesity or demonstrate a reduction in body weight in those patients administered the amylin agonist. Furthermore, Kolterman 1996 is silent with regard to the effect of the amylin agonist on body weight. Kolterman 1996 does not report the weight of the subjects at the end of the study and nothing in the reference indicates that pramlintide had any effect on the weight of the subjects.

Furthermore, the Examiner asserts (Office Action, page 26, lines 27-28) that "the very active step recited in the instantly claimed method was disclosed and practice by Kolterman et al. in April, 1996." Applicants respectfully disagree with this assertion. The patient population of Kolterman 1996 is not necessarily the same as the claimed subject, i.e., a subject in need of a method of treating obesity. The Examiner has provided no extrinsic evidence to show that these patient populations are one in the same. Furthermore, Applicants respectfully note that the "fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." In re Rijckaert, 9 F.3d 1531, 1534 (Fed.

Cir. 1993); emphasis in original. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the references, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " In re Robertson 169 F.3d 743, 745 (Fed. Cir. 1999); emphasis added.

Specifically, the courts have held that the phrase "in need thereof" (e.g., as recited in independent Claims 1, 7, 14 and 16) is meaningful, and that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose." Jansen v. Rexall Sundown, Inc. 342 F.3d 1329, 1333 (Fed. Cir. 2003). Thus, Kolterman 1996 cannot render unpatentable the subject population of the claimed invention. Thus, Kolterman 1996 does not provide each and every element of the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

Claims 7,14 and 16

The rejection of Claims 7, 14 and 16 under 35 U.S.C. § 102(e)(2) (Office Action, page 27, item 48) for alleged anticipation over U.S. 5,321,008 ('008 patent) as evidenced by Tsanev (Id.) is respectfully traversed.

The claimed invention as exemplied in Claims 7, 14 and 16 is directed to methods of treating obesity in a human subject in need of such treatment through administration of an amylin or an amylin agonist. In contrast, as acknowleged by the Examiner (Office Action, page 28, lines 13-14), the '008 patent describes "a method of treating diabetes mellitus in an insulin-requiring human who suffers from Type 1 or Type 2 diabetes mellitus..." The '008 patent is silent with respect to obesity, treatment of obesity, or identification of a population in need of treatment for obesity. In an attempt to cure the deficiency in the '008 patent, the Examiner relies on Tsanev to provide alleged evidence that 80-90% of diabetic patients are obese. However, 80-90% falls short of the 100% (i.e., always, under any circumstanes) criterion required by the claims and required by the law as discussed in the respone to Office Action item 38 above. See e.g., Schering Corp. v. Geneva Pharms., Inc., Id.; Abbott Laboratories v. Baxter Pharmaceutical Products, Inc., Id.) Thus, the '008 patent does not provide each and every element of the claimed

invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the present rejection.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that are otherwise provided for in the documents accompanying this paper. However, if any additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required thereof (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account Number 50-2387, referencing docket number 18528.231. Applicant(s) likewise authorize a charge to Deposit Account Number 50-2387 for any other fees related to the present application that are not otherwise provided for in the accompanying documents.

Respectfully submitted,

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